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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/502,065 | 01/18/2005 | W Wayne Lautt | 14233.17USWO | 2089 |

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

| EXAMINER | |
|---|---|
| GUDIBANDE, SATYANARAYAN R | |
| ART UNIT | PAPER NUMBER |
| 1654 | |

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/502,065 | LAUTT ET AL. | |
| | Examiner | Art Unit | |
| | Satyanarayana R. Gudibande | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *6-18,21-25 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *18 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-17,21,23-25 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/6/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 6-18 21-25, 29-31 are pending.

Claims 6-17, 21, 23, 24(in-part to the extent that the claim reads on non-insulin dependent diabetes), 25, 29-31 are examined on merit.

Claims 18 and 22 have been withdrawn as being drawn to non-elected species.

### *Election/Restrictions*

Applicant's election with traverse of group II invention (claims 6-8, 11, 29 and 30) and election of N-acetylcysteine and SIN-1 as species in the reply filed on 8/11/06 is acknowledged. The traversal is on the ground(s) that the unity of invention exists between the inventions in the instant application and the combination of an independent claim for a product and an independent claim for a use of said product constitutes one invention. Applicants have requested rejoinder of groups II and III. Applicants further argue that the reference cited to break the unity of invention is inappropriate, as the reference does not teach the presence of both cysteine and nitrosylated cysteine in physiologic buffer. This has not been found to be persuasive, the reference clearly states that the nitrosylated cysteine is formed in the presence of N2O3 present in the buffer. Therefore, the reference does teach the presence of cysteine and nitrosylated cysteine and hence the special technical feature of claim 6 is not a contribution over the prior art.

Applicants request to rejoin inventions II and III has been considered. In view of the amendments to the claims, the inventions II and III will be rejoined, all claims with the exception of 24 will be examined on the merit. Claim 24 will be examined to the extent that the method

reads on the non-insulin dependent diabetes will be examined on merit. In a telephone conversation with Mr. Brian Dorn, on August 28, 2006, the above agreement was reached.

The requirement is still deemed proper and is therefore made FINAL.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-8, 29 and 30 rejected under 35 U.S.C. 102(b) as being anticipated by US 6,436,996 B1 issued to Vitek, et al.

In the instant application, applicants claim a pharmaceutical composition comprising of N-acetylcysteine and SIN-1 (elected species) as glutathione increasing and nitric oxide increasing compounds.

Vitek, et al., discloses such a composition comprising SIN-1 and N-acetylcysteine. Although, Vitek, et al., discloses the composition comprising of SIN-1 and N-acetylcysteine (claim 1, column 9, lines 5-8) as an exogenous source of increasing the nitric oxide levels in cells in Alzheimer's patients who suffer from decreased nitric oxide levels associated with the presence of APOE4 alleles, the composition comprises of the species elected in the present invention and hence, when administered, should perform the desired function of glutathione increasing and nitric oxide increasing functions (meeting the limitations of claims 6 and 7) in

liver. Further, the composition contains the presence of cysteine and dithiothreitol, which are known anti oxidants, meets the limitation of claim 8.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-17, 21, 23-25, 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,436,996 B1 issued to Vitek, et al., in view of Mattia, et al., Diabetologia, 1998, 41, 1392-1396 and further in view of WO 00/19992 of Lautt, et al.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In the instant application, applicants claim a pharmaceutical composition comprising of N-acetylcysteine and SIN-1 and a method of administering the pharmaceutical composition for reducing insulin resistance in a mammalian patients having lower than normal glutathione

concentration wherein, N-acetylcysteine acts as glutathione increasing compound and SIN-1 acts as the nitric oxide increasing compound.

Vitek, et al., discloses composition containing the N-acetylcysteine and SIN-1 (claim 1, column 9, lines 5-8) as an exogenous source of increasing the nitric oxide levels in cells in Alzheimer's patients who suffer from decreased nitric oxide levels associated with the presence of APOE4 alleles. Even though the disclosed composition is for increasing the exogenous nitric oxide level in Alzheimer's patients, the disclosed composition will have desired inherent properties that cannot be precluded in the instant application since the compounds are same. The composition disclosed by Vitek, et al., meets the limitations of 6-8, 14, 15, 21, 23, 29 and 30. The reference does not teach that the composition is for a method of reducing insulin resistance in a patient having lower than normal hepatic glutathione levels.

Mattia, et al., have shown that administration of N-acetylcysteine increases the glutathione and GSH/GSSG ratio concentration in non-insulin dependent diabetic patients (column 2 of 'summary' on page 1392). Lautt, et al., teaches the administration of nitric oxide increasing compounds such as SIN-1 stimulates nitric oxide in liver (abstract and page 8, lines 11-15) and provides a method for increasing insulin sensitivity (reducing insulin resistance). The reference of Mattia (column 2, page 1394 paragraph 1; and bridging paragraph on page 1395) and Lautt (pages 12-14) indicates that the respective compounds can be administered orally and intravenously (meeting the limitations of claims 16 and 17) to human patients. Lautt also describes the composition of the active ingredient along with other pharmaceutically acceptable carriers, diluents and adjuvants and vehicles (page 12, lines 4-17). The reference further

discloses the use of targeted delivery systems such as vectors, liposomes, polymer matrices and microspheres (page 14, lines 7-13) meeting the limitations of claims 11 and 30.

It would have been obvious to one skilled in the art to combine the methods taught by Vitek, Mattia and Lautt to design a method for the treatment of non-insulin dependent diabetes. The motivation comes from the fact that the mechanism of non-insulin dependent diabetes involves both increase in glutathione concentration and a nitric oxide enhancement. Mattia teaches the use of N-acetylcysteine for increasing the glutathione concentration and Lautt teaches the use of SIN-1 for increasing the nitric oxide concentration in treating the non-insulin dependent diabetes. Even though Vitek used the combination of N-acetylcysteine and SIN-1 for a disease condition such as Alzheimer's, the reasonable expectation of success was provided by this reference. Vitek was successful in using the combination of the drugs to increase the nitric oxide levels in cells such as Alzheimer's disease. Therefore, the invention as a whole was clearly prima facie obvious to one skilled in the art at the time the invention was made. As set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; the idea of combining them flows logically from their having been individually taught in prior art."

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of the claim with the phrase "a pharmaceutically acceptable liver-targeting substance" renders the claim indefinite. Although, the specification (page 10, line 1-11) mentions compounds such as albumin, liposomes and bile salts, it is inadequate because, the recitation of the claim implies any and all compounds that is taken up the liver when administered with the desired compound. Hence the claims are indefinite failing to particularly point out and distinctly claim the subject matter which applicant regards as invention.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Satyanarayana R. Gudibande, Ph.D.
Art Unit 1654

ANISH GUPTA
PRIMARY EXAMINER